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09/701,623	12/01/2000	Chang Yi Wang	1151-4153US1	8939

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EXAMINER

HUYNH, PHUONG N

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/701,623	Applicant(s) WANG ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 3-18 and 21-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2 and 19-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-28 are pending.
2. Applicant's election with traverse of Group I, Claims 1-2 and 19-20 drawn to SEQ ID NO: 5, an IgE-CH3 domain antigen peptide between about 25 and 29 amino acids in length, homologous sequence, crossreactive and immunologically functional analogs thereof, filed 6/20/02, is acknowledged. The traversal is on the grounds that (1) the claims are directed to the use of a single epitope in IgE-CH3 domain conjugated to a Th epitope to generate antibodies against IgE for the treatment of allergies, (2) SEQ ID NO: 5, 6, 7, 8 and 84 are modified sequence of a single epitope in IgE-CH3 domain from humans, dog, rat, mouse and horse, respectively conjugated to a promiscuous Th epitope selected from the group consisting of SEQ ID NO: 9-12, 60-82 and 89 and the conjugates may further be conjugated with an invasin domain to further improve the immunoresponse and (2) it would be a burdensome for the Applicants to file 60 different applications for the different permutations that applicant have taught and described. Upon reconsideration, the peptides (SEQ ID NO: 6-8 and 84) of Groups II-V have been rejoined with Group I since these peptides (SEQ ID NO: 6-8 and 84) are homologue and analog of human IgE-CH3 domain. Therefore, the requirement of Group I (now claims 1-2) that read on SEQ ID NO: 5-8 and 84 and Groups VI-LX is still deemed proper and is therefore made FINAL.
3. Claims 3-18 and 21-28 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.
4. Claims 1-2 and 19-20, drawn to an IgE-CH3 domain antigen peptide selected from the group consisting of SEQ IDNO: 5-8, and 84, homologous sequences from the epsilon heavy chain of mammalian IgE-CH3, and analog thereof are being acted upon in this Office Action.
5. The disclosure is objected to because of the following **informality**: (1) incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference. Therefore the embedded hyperlinks and/or other forms of browser-executable code disclosed on page 4, line 7, page 25, line 26, and

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page 44, line 7 of the instant specification are impermissible and require deletion. Where the hyperlinks and/or other forms of browser-executable codes are part of applicant's invention and are necessary to be included in the patent application in order to comply with the requirements of 35 U.S.C. 112, first paragraph, and applicant does not intend to have these hyperlinks be active links, then this objection will be withdrawn and the Office will disable these hyperlinks when preparing the patent text to be loaded onto the PTO web database. Appropriate action is required.

6. Applicant should amend the first line of the specification to reflect the relationship between the instant application and PCT/US99/13959 filed December 6/21/1999 as stated on the oath.
7. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d), a certified copy of the certified priority document must be submitted in reply to this action.
8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
9. Claims 1 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, selected from the group consisting of SEQ ID NO: 5-8 and 84, (2) a homologous sequence from the epsilon heavy chain of mammalian IgE-CH3 and a crossreactive and an immunologically functional analog of IgE-CH3 domain antigen peptide between about 25 and about 29 amino acid in length containing two cysteine residues separated by about 23 amino acids residues, selected from the group consisting of SEQ ID NO: 6-8 and 84, and (3) an IgE-CH3 domain antigen peptide selected from the group consisting of SEQ ID NO: 5-8 and 84 for treating allergy, **does not** reasonably provide enablement for (1) *any* IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs thereof" for treating allergy, (2) *any* peptide conjugate comprising a carrier protein covalently attached to one or more of *any* IgE-CH3 domain antigen peptide between

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about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs" thereof for treating allergy, (3) *any* peptide conjugate comprising a carrier protein covalently attached to one or more of *any* IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs" thereof for treating allergy wherein the carrier protein is keyhole limpet hemocyanin for treating allergy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only the full length IgE polypeptide from human (SEQ ID NO: 1), dog (SEQ ID NO: 2), rat (SEQ ID NO: 3), and mouse (SEQ ID NO: 4). The specification further discloses various modified IgE CH3 domain antigen peptides from human such as the ones disclosed in Table 2 either having a native Cysteine at position 358 or 312 or 418 of SEQ ID NO: 1 conservatively substitute with a serine (SEQ ID NO: 28-35) or having a cysteine residue inserted at the N and the C terminal of CH2, CH3 or CH4 domain. The peptides mentioned above are covalently crosslinked with a carrier molecule such as KLH by conventional glutaraldehyde or MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester or helper T epitope such as SEQ ID NO: 10-13, and the ones shown in Tables 5 and 6 where CH3 domains are crosslinked to Th helper epitope or Invasin domain. The specification discloses cyclic peptide. The peptides shown in Table 2 are screened for cross-reactivity with human IgE (Table 2 on pages 69-73) and inhibition of histamine release (Table 3 on page 74). The specification further

discloses that only anti-IgE antibodies generated from peptide of SEQ ID NO: 5 crossed linked to the specific synthetic Th epitope (Th (1,2,4)- or invasin-GG-Synthetic T helper epitope (1,2,4)-GG- (Table 5) significantly inhibit Histamine release while anti-IgE antibody generated from other peptides such as SEQ ID NO: 28-38 crosslinked to KLH or crosslinked to Th epitope such as SEQ ID NO: 46, 55 and 57 do not inhibit histamine release (Table 3).

The specification does not teach how to make and use *any* homologues sequences from the epsilon heavy chain of *any* mammalian IgE-CH3 for treating allergy such as inhibiting histamine release because there is no structure associated with homologous sequences without SEQ ID. Even if the homologous sequences are known, they are not necessary have the same biological functions as applicant demonstrated in Table 2 and 3, in turn, would be useful for treating allergy. Given the indefinite number of undisclosed homologous sequences, it is unpredictable which undisclosed homologous sequences would have the same structure as the claimed sequence, in turn, would be useful for treating allergy such as inhibits histamine release without inducing anaphylaxis.

With regard to *any* crossreactive and immunological functional analogs thereof, the term "analog" can be DNA, RNA, protein, and small organic and inorganic molecule. There are insufficient guidance and working examples in the specification demonstrating that any undisclosed analog would be the same structure and function as SEQ ID NO: 5-8 and 84, in turn, would be useful for treating allergy. Even if the sequence is known, there is insufficient guidance in the specification as to what type and number of amino acids within the full length amino acid sequence (polypeptide) of SEQ ID NO: 1-4, can be added, deleted, substituted and whether after modification would retain both structure and function and be useful for treating allergy.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Consistent with applicant's own disclosure, not all modified analogs such as the ones listed in Table 2 and 3 are useful for inhibiting histamine release. Further, the term "analog" does not convey the structure. Given the indefinite number of undisclosed analog, it is unpredictable which undisclosed analog would be the same structure and function as the peptides selected from the group consisting of SEQ ID NO: 5-8 and 84, in turn, would be useful for any purpose. Since the "homologue sequence" and "immunologically functional analogs" are not enabled, it follows that any peptide

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conjugate comprising said "homolog sequence" and "analog" covalently attached to a carrier protein such as keyhole limpet hemocyanin is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

10. Claims 1 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs thereof" for treating allergy, (2) *any* peptide conjugate comprising a carrier protein covalently attached to one or more of *any* IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs" thereof for treating allergy, (3) *any* peptide conjugate comprising a carrier protein covalently attached to one or more of *any* IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acids residues, wherein the peptide is *any* "homologues sequences" from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* "crossreactive and immunological functional analogs" thereof for treating allergy wherein the carrier protein is keyhole limpet hemocyanin fir treating allergy.

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The specification discloses only the full length IgE polypeptide from human (SEQ ID NO: 1), dog (SEQ ID NO: 2), rat (SEQ ID NO: 3), and mouse (SEQ ID NO: 4). The specification further discloses various modified IgE CH3 domain antigen peptides from human such as the ones disclosed in Table 2 either having a native Cysteine at position 358 or 312 or 418 of SEQ ID NO: 1 conservatively substitute with a serine (SEQ ID NO: 28-35) or having a cysteine residue inserted at the N and the C terminal of CH2, CH3 or CH4 domain. The peptides mentioned above are covalently crosslinked with a carrier molecule such as KLH by conventional glutaraldehyde or MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester or helper T epitope such as SEQ ID NO: 10-13, and the ones shown in Tables 5 and 6 where CH3 domains are crosslinked to Th helper epitope or Invasin domain. The specification discloses cyclic peptide. The peptides shown in Table 2 are screened for cross-reactivity with human IgE (Table 2 on pages 69-73) and inhibition of histamine release (Table 3 on page 74). The specification further discloses that only anti-IgE antibodies generated from peptide of SEQ ID NO: 5 cross linked to the specific synthetic Th epitope (Th (1,2,4)- or invasin-GG-Synthetic T helper epitope (1,2,4)-GG- (Table 5) significantly inhibit Histamine release while anti-IgE antibody generated from other peptides such as SEQ ID NO: 28-38 crosslinked to KLH or crosslinked to Th epitope such as SEQ ID NO: 46, 55 and 57 do not inhibit histamine release (Table 3).

With the exception of the specific peptides mentioned for treating allergy, there is insufficient written description about the structure associated with function of *any* homologues sequences from the epsilon heavy chain of *any* mammalian IgE-CH3 and *any* crossreactive and immunological functional analogs thereof for treating allergy. Further, applicant discloses only five IgE-CH3 domain from human, mouse, rat, dog and horse and functional analogs from only human IgE-CH3. There are no additional homologues sequences from the epsilon heavy chain of *any* other mammalian IgE-CH3 and *any* other crossreactive and immunological functional analogs that are useful for inhibiting histamine release. Thus, Applicant was not in possession of the claimed genus. See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398. Since the "homolog sequence" and "immunologically functional analogs" are not adequately described, it follows that *any* peptide conjugate comprising said "homolog sequence" and "analog" covalently attached to a carrier protein such as keyhole limpet hemocyanin are not adequately described.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

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11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 1-2 and 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of " IgE-CH3 domain antigen peptide" in claims 1 and 2 are ambiguous and indefinite because the specification discloses a peptide antigen consisting of the amino acids 413-435 from the CH3 domain of human IgE of SEQ ID NO: 1.

The recitation of " immunologically functional" in claim 1 is ambiguous, indefinite and one of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention because it is not clear what is meant by "immunologically functional" since an increase in histamine release, for example, would still be considered "immunological functional".

Appropriate correction is required.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

14. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Navarro *et al* (Molec Immunol 32: 1-8, 1995; PTO 892).

Navarro *et al* teach various homologous sequences from the epsilon heavy chain of mammalian IgE-CH3 such as human, sheep, mouse, and horse (See Figs 2 & 3, in particular) and all cysteine residues in the horse, which are essential for maintaining the overall structural features of Ig domains, are found in the same positions as in human, chimpanzee, orangutan and the sheep (See page 6, column 2, first full paragraph, in particular). Navarro *et al* further teach

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the ligands for the FcεRIII are located primary in the Cε domain of IgE (See page 7, column 1, in particular). Thus, the reference teachings anticipate the claimed invention.

15. Claims 1 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghaderi *et al* (Mol Immunology 30(18): 1655-63, 1993; PTO 892).

Ghaderi *et al* teach various immunologically functional analogs from the human epsilon heavy chain IgE-CH3 domain such as Y137 and Y136 (See Table 1, in particular) that inhibit the binding of IgE to an FcεRII/CD23 positive cell line (See page 1658, Results, and Fig 2. Ghaderi *et al* further teach various functional analogs such as peptide Y137, which represents residues 364-383 of the human IgE domain and peptide analog Y136, which represents residues 401-415 of the human IgE domain (See Table 1, in particular). Ghaderi *et al* further teach a peptide conjugate such as human epsilon heavy chain IgE-CH3 domain such as Y137 and Y136 covalently linked (conjugated to) a carrier peptide such as keyhole limpet hemocyanin (KLH) (See page 1657, column 1, last paragraph, in particular). Thus, the reference teachings anticipate the claimed invention.

16. Claims 1-2 and 19-20 are rejected under 35 U.S.C. 102(e) (2) as being anticipated by US Pat No. 6,025,468 A (Feb 2000, PTO 892).

The '468 patent teaches a peptide such as SEQ ID NO: 95 that is 25 amino acid in length, which is between about 25 and about 29 amino acids in length and the reference peptide contains two cysteine residues separated by 23 amino acid residues (See entire document, SEQ ID NO: 95 of '468 patent). The reference peptide is 100% identical to the claimed peptide of SEQ ID NO: 5. The reference peptide is inherently an IgE-CH3 domain antigen peptide. The '468 patent further teach a peptide conjugate such as keyhole limpet hemocyanin (KLH), which is a carrier protein, covalently linked (conjugated) to the reference peptide (See column 16, line 34, in particular). Thus, the reference teachings anticipate the claimed invention.

17. Claims 1-2 and 19-20 are rejected under 35 U.S.C. 102(e) (2) as being anticipated by US Pat No. 6,228,987 B1 (May 2001, PTO 892).

The '987 patent teaches a peptide such as SEQ ID NO: 95 that is 25 amino acid in length, which is between about 25 and about 29 amino acids in length containing two cysteine residues separate by 23 amino acid residues (See entire document, SEQ ID NO: 95 of '987 patent). The

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reference peptide is 100% identical to the claimed peptide of SEQ ID NO: 5. The '987 patent further teach a peptide conjugate such as keyhole limpet hemocyanin (KLH), which is a carrier protein, covalently linked (conjugated) to the reference peptide (See column 16, line 34, in particular). Thus, the reference teachings anticipate the claimed invention.

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Navarro *et al* (Molec Immunol 32: 1-8, 1995; PTO 892) in view of Ghaderi *et al* (Mol Immunology 30(18): 1655-63, 1993; PTO 892).

The teachings of Navarro *et al* have been discussed supra.

The claimed invention as recited in claim 1 differs from the reference only that an IgE-CH3 domain peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acid residues.

Ghaderi *et al* teach various functional analogs from human IgE CH3 domain such as peptide Y137 spanning residues 364-383 of the human IgE CH3 domain, which is 19 amino acids in length and peptide Y136 spanning residues 401-415 of human IgE CH3 domain, which is 14 amino acid residues in length (See page 1656, Table 1, in particular). The reference peptides together are 33 amino acids in length, which is about 19 amino acids in length and capable of inhibiting the binding of IgE to an FcεRII/CD23 positive cell line (See page 1658, Results, Figs 2

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and 3, in particular). Ghaderi *et al* further teach despite being linearly separated as seen from the numbering of residues, the Y136 and Y137 peptides sequences are continuous within the two parallel complementary beta strands and are closely oriented within the 3-dimensional IgE structure, indicating that the IgE molecules interact with the FcεRII/CD23 receptor are at two different, closely related, epitopes within the CH3 domain and are important for triggering of mast cells to release histamine (See page 1661, column 2, first paragraph, page 1662, in particular). Ghaderi *et al* teach the antisera to peptides Y137 and Y136 of the CH3 domain conjugated to KLH recognized IgE bound to the B cells, indicating that the reference amino acid residues spanning from 364 to 415 are important and involved in IgE binding (See page 1660, column 1 bridging column 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make functional peptide analogs in the IgE-CH3 domain as taught by Ghaderi *et al* using the various mammalian sequences as taught by Navarro *et al* for an IgE-CH3 domain antigen peptide between about 25 and about 29 amino acids in length containing two cysteine residues separated by about 23 amino acid residues as taught by Ghaderi *et al* and Navarro *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Ghaderi *et al* teach amino acid residues from 362 to 415 of the IgE CH3 domain are important for IgE binding to the FcεRII/CD23 receptor on B cell (See page 1660, column 1 bridging column 2, in particular). Navarro *et al* teach the cysteine residues are essential for maintaining the overall structural features of Ig domains, and are found in the same positions as in human, chimpanzee, orangutan and the sheep (See page 6, column 2, first full paragraph, in particular).

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21. Claims 1, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Navarro *et al* (Molec Immunol 32: 1-8, 1995; PTO 892) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1998, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 82-3 and 128-129).

The teachings of Navarro *et al* have been discussed supra.

The claimed invention as recited in claim 19 differs from the reference only that a peptide conjugate comprising a carrier protein covalently attached to one or more IgE-CH3 domain antigen peptides.

The claimed invention as recited in claim 20 differs from the reference only that the peptide conjugate wherein the carrier protein is keyhole limpet hemocyanin.

Harlow *et al* teach a peptide conjugate such as coupling any antigen to a protein carrier such as keyhole limpet hemacyanin (KLH) with a heterobifunctional crosslinker such as m-Maleimidobenzoyl-hydroxysuccinimide ester (See page 82-83, page 129, in particular). Harlow *et al* teach that any peptides that are not immunogenic can be made more immunogenic by coupling to a carrier such as keyhole limpet hemacyanin (KLH) (See page 129, second paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate the various homologous sequences from the epsilon heavy chain of mammalian IgE-CH3 such as human, sheep, mouse, and horse as taught by Navarro *et al* to a carrier protein such as keyhole limpet hemacyanin (KLH) as taught by Harlow *et al* for a peptide conjugate comprising a carrier protein covalently attached to one or more IgE-CH3 domain antigen peptides as taught by Navarro *et al* and Harlow *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because Harlow *et al* teach any peptides that are not immunogenic can be made more immunogenic by coupling to a carrier such as keyhole limpet hemacyanin (KLH) (See page 129, second paragraph, in particular).

22. SEQ ID NOS: 6-8 and 84 are free of art.

23. No claim is allowed.

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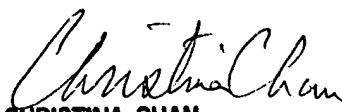
24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.
25. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.

Patent Examiner

Technology Center 1600

September 9, 2002


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TECHNOLOGY CENTER 1600